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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,943	03/02/2004	William R. Wilson	8654/2222	2176

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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 11/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/790,943	WILSON ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/15/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Claims 1-23 are presented for prosecution on the merits.

Information Disclosure Statement(s)

Applicant's Information Disclosure Statement received April 15, 2004 has been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

Claim Rejection(s)—35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1, 3, are rejected under 35 U.S.C. 102(b) as being anticipated by Cliffe et al.

Cliffe et al. disclose a method of injecting mice having mammary tumours with a combination of DMXAA and a nitrogen mustard (i.e. alkylating agents) such as SN23862 or SR 4233. Cliffe et al. Disclose that the combination treatment leads to enhanced anti-tumor effect. Please see the abstract; page 375, first column, first full paragraph; pages 375-376.

Claim Rejection(s)—35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siemann et al.

Siemann et al. disclose methods of treating sarcoma, breast and ovarian tumors with a combination of DMXAA and cisplatin or cyclophosphamide. Results of the methods demonstrate that when DMXAA is combined with these conventional chemotherapeutics, tumor cell kill was increased 10-500-fold compared to that seen with chemotherapy alone. Please see the abstract.

Siemann et al. do not disclose (1) administration of DMXAA and cisplatin or cyclophosphamide to a mammal, (2) specific compostions or pharmaceutical compositions containing a combination of DMXAA and cisplatin and cyclophosphamide or (3) a kit for separate administration of DMXAA and cisplatin or cyclophosphamide.

However, concerning item (1), it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the combination of DMXAA and cisplatin or cyclophosphamide to a patient suffering from sarcoma, ovarian or breast cancer because, based on the desirable enhanced tumor cell kill demonstrated in the methods of Siemann et al., one of ordinary skill in the art would reasonably expect the combination of DMXAA and cisplatin or cyclophosphamide to exhibit cytotoxicity against the tumors in a mammalian patient. Thus, such a modification would have been motivated by the reasonable expectation that mammals suffering from sarcoma, ovarian or breast cancer would be treated when administered DMXAA and cisplatin or cyclophosphamide.

With respect to compositions, including pharmaceutical compositions, as well as kits comprising DMXAA and cisplatin or cyclophosphamide, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a composition, pharmaceutical product or kit by combining DMXAA and cisplatin or cyclophosphamide because one of ordinary skill in the art would reasonably expect these compositions or kits to be useful therapeutically based on Siemann's teaching that the two compounds together exhibit enhanced anti-tumor activity.

In addressing claims 2 and 3, it would have been obvious to one of ordinary skill

in the art to administer the two compounds in such a manner as to optimize therapeutic efficacy. Moreover, with respect to claims 8, 12, 13, 17 and 21, since therapeutic efficacy is dependent upon the effective amounts or concentration of the active agents, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the compositions and kits such that DMXAA and cisplatin or cyclophosphamide are present to exihibit optimum anti-tumor activity. Finally, modification of the pharmaceutical composition into a form suitable for intravenous administration would have been obvious since one of ordinary skill in the art would reasonably expect an intravenous formulation to effectively deliver DMXAA and cisplatin and cyclophosphamide to a patient in need thereof.

3. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson 6,667,337 in view of Siemann et al., supra or Zhou et al.

Wilson discloses a method of treating cancer in a mammal, the method comprising administering to the mammal a pharmaceutical composition containing DMXAA and paclitaxel or docetaxel. The compounds may be administered sequentially or simultaneously and the compounds may be administered intravenously. Please see the abstract; col. 2, lines 46-52; col. 3, lines 19-60.

Wilson does not disclose combining DMXAA with cisplatin, cyclophosphamide or vincristine; however, the Examiner refers to (1) Siemann et al., which disclose methods of treating sarcoma, breast and ovarian tumors with a combination of DMXAA and cisplatin or cyclophosphamide, wherein when DMXAA is combined with these conventional chemotherapeutics, tumor cell kill was increased 10-500-fold compared to

that seen with chemotherapy alone (abstract) or (2) Zhou et al., which studied the effects of vincristine, vinblastine, etc. on DMXAA metabolism by human liver microsomes, concluding that these conventional anti-cancer agents appear unlikely to alter the pharmacokinetics of DMXAA in vivo (please see page 133; abstract, Conclusion).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method and composition of Wilson to substitute paclitaxel/docetaxel with cyclophosphamide or cisplatin because, based on the desirable enhanced tumor cell kill demonstrated in the methods of Siemann et al., one of ordinary skill in the art would reasonably expect the combination of DMXAA and cisplatin or cyclophosphamide to exhibit cytotoxicity against the tumors in a mammalian patient. Thus, such a modification would have been motivated by the reasonable expectation that mammals suffering from cancers such as sarcoma, ovarian or breast cancer would be treated when administered DMXAA and cisplatin or cyclophosphamide.

Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method and composition of Wilson to substitute paclitaxel/docetaxel with vincristine because one of ordinary skill in the art would reasonably expect the combination of DMXAA and vincristine to demonstrate effective anti-tumor activity since Zhou et al. teach that vincristine would not interfere with the pharmacokinetic activity of DMXAA when administered to a mammal.

With respect to kits comprising a combination of DMXAA and (a) cisplatin or

cyclophosphamide or (b) vincristine, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a kit because one of ordinary skill in the art would reasonably expect the kit to be useful therapeutically.

In addressing claim 2, it would have been obvious to one of ordinary skill in the art to administer the two compounds in such a manner as to optimize therapeutic efficacy. Moreover, with respect to claims 8, 13, 17 and 21, since therapeutic efficacy is dependent upon the effective amounts or concentration of the active agents, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the compositions and kits such that DMXAA and cisplatin/ cyclophosphamide or vincristine are present to exhibit optimum anti-tumor activity.

Conclusion

Claims 1-23 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybille Delacroix-Muirheid** whose telephone number is **571-272-0572**. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Christopher Low**, can be reached on **571-272-0951**. The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM
Oct. 26, 2004

Cybille Delacroix-Muirheid
Patent Examiner Group 1600